REMARKS

Petition under 37 C.F.R. 1.78:

Applicants have filed a petition under 37 CFR 1.78 requesting that a priority claim to U.S. provisional application No. 60/085,764, filed May 16, 1998 be granted.

Objection of the claims:

Claim 6 has amended to obviate the rejection. Specifically, claim 6 has been amended to make the claim properly dependent on claim 5.

Rejection of the claims under 35 U.S.C. §112

Claims 1 has been rejected under 35 U.S.C. 112, first paragraph. The Examiner points out, and the Applicants acknowledge, that there are many different types of physiological conditions present in different mammals and in different tissues of a mammal. Applicants have therefore amended the claims to specify that the disulfide bond is cleaved inside a mammalian cell in the cytoplasm of the cell. The specification describes transduction signals for transporting a compound across a cell membrane (page 25 lines 29-30.) Whether the compound is initially outside the cell, or has been endocytosed and is therefore in an intracellular vesicle, transport of the compound across a membrane by a transduction signal delivers the compound to the cell cytoplasm. Applicants demonstrate that the described bonds are labile under conditions similar to mammalian cytoplasmic conditions. Applicants further demonstrate that an activated disulfide bond between a transduction signal and a fluorophore is cleaved inside a mammalian cell (example 10). While different cells in a mammal may reside in a variety of extracellular conditions, the cytoplasm of a mammalian cell does not vary widely from one cell type to another in a mammal or from one mammal to another.

Rejection of the claims under 35 U.S.C. §102

Claims 1, 5 and 6 have been rejected under 35 U.S.C. 102 (a/b/e) as being anticipated by Bulaj *et al.* and Keire *et al.* Applicants have amended the claim to obviate the rejection. Specifically, the claims have been amended to claim a transduction peptide linked to molecule via an activated disulfide bond for delivery of the molecule to a mammalian cell. Neither Bulaj *et al.* or Keire *et al.* teach a molecule linked to a transduction signal via an activated disulfide bond for delivery of the molecule to the cytoplasm of a cell.

Claims 1, 2, 5, 6 and 13 have been rejected under 35 U.S.C. 102 (c) as being anticipated by Stein *et al.* (6,528,774). Applicants have amended the claims to obviate the rejections. Support for "said molecule covalently linked to a transduction signal" and "said transduction signal transports said molecule to said cytoplasm of said cell" can be found in the specification on page 25 line 29 to page 26 line 10, in example 6 on page 37, and in example 10 starting on page 38. Support for "cleavage of said disulfide bond in said cell enhances delivery of said molecule to the cytoplasm of said cell" can be found in the specification in example 10 starting on page 38.

The Action states that the definition of transduction signal in the specification does not exclude various mechanism, such as endocytosis, from transporting a compound across a membrane of a cell. Applicants respectfully disagree. The process of endocytosis does not transport a molecule across a membrane. In the process of endocytosis, an invagination is formed in the membrane which ultimately separates from the membrane to form a membrane enclosed vesicle. While an endocytosed compound is moved from the exterior of a cell to the interior of a cell, the molecule remains inside a membrane enclosed compartment, the endocytic vesicle, and remains on the same side of the membrane. The compound is moved "across" the plasma membrane with respect to the cell, but is not moved across the membrane with respect to the membrane itself. Thus, a ligand or cell uptake promoter as used by Stein *et al.* and Monahan *et al.* (6,429,200) is not equivalent to a transduction signal.

Claims 1, 5, 6, and 13 have been rejected under 35 U.S. C. 102 as being anticipated by (102(e)) or invented by (102(f)) Monahan *et al.* (6,429,200). Applicants have amended the specification to claim priority from provisional application 60/085,764, filed on May 16, 1998 to obviate the rejection. A petition under 37 CFR 1.78 has been filed requesting that the a priority claim to U.S. provisional application No. 60/085,764, filed May 16, 1998 be granted along with a statement that the entire delay in filing the priority claim was unintentional. A replacement page 1 of the specification in enclosed that indicates the priority claim.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1-6 and 13 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being sent by facsimile transmission to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on this date: 5/21/2004.

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